Claims 1-23 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to and claims 13 and 14 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR §§ 1.801-1.809.

It is unclear if cell lines which produce antibodies having the exact chemical identity and properties of the antibodies designated LMH-1, LMH-2, or LMH-3 are known and publicly available, or can be reproducibly isolated without undue experimentation. Accordingly, filing of evidence of the reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above cell lines, one of skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: the claimed cell line; the cell lines which produce the chemically and functionally distinct antibodies claimed; and/or, the claimed antibody's amino

acid or nucleic acid sequence is an unpredictable event. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found on antibodies having different specificities. Therefore, it would require undue experimentation to reproduce the claimed monoclonal antibody species chemically as produced by the hybridomas designated LMH-1, LMH-2, or LMH-3. A suitable deposit of the hybridomas would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See the criteria set forth in 37 CFR §§ 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty, that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the deposited biological materials will be replaced should they become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR §§ 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
(d) the deposits were viable at the time of deposit; and,
(e) the deposits will be replaced if they should become non-viable.

Applicant is also reminded that information regarding the deposits, such as the name and address of the depository, in addition to the accession numbers of the deposits and the date(s) of the deposits, **must** be added to the specification by means of filing an amendment as required by 37 CFR § 1.809(d).

Claims 1-3, 5-7, and 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anti-idiotypic antibodies specific for the Hu3S193 monoclonal antibody, does not reasonably provide enablement for anti-idiotypic antibodies (anti-id) specific for anti-Lewis Y (LeY) monoclonal antibodies generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Anti-id antibodies require a parent antibody and applicant does not disclose or enable the full scope of anti-LeY monoclonal antibodies for use in the invention of the scope as claimed. As set forth above, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity. Thus, an anti-id antibody specific for one anti-LeY does not provide an indication that that anti-id antibody predictably binds to any other anti-LeY antibody (see e.g. the results of Hirashima et al. (J. Immunol. 145: 224, 1990) at page 226, col. 1, and the discussion of public and private idiotopes). One would simply not be assured of the ability to predictably make and use products of the scope as claimed.

Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification teaches analysis of serum samples with an immobilized anti-Lewis Y monoclonal antibody on a sensor chip for determination of anti-humanized antibody response. There would appear to be essential undisclosed steps in the method as instantly claimed. One would not be able to detect an anti-humanized antibody response with the method as instantly claimed because a patient treated with the antibody may have circulating antibody that would block binding of any added antibody and any reduction in binding of the labeled antibody would have nothing to do with an anti-humanized antibody response in the patient. Applicant is requested to direct the Examiner's attention to specific passages where support for the method as now suggested by this claim can be found in the specification as filed. Absent further written description and guidance from applicant, one would not be assured of the predictable ability to practice the method as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3-8, and10-23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2 and claims dependent thereupon, "the" variable region lacks antecedent basis and is not clear as to what applicant intends as encompassed because an antibody has multiple complementarity determining regions in the variable portions of both the heavy and light chains.

In claim 3 and claims dependent thereupon, "the" binding lacks antecedent basis.

In claims 4, 16, 19, 22, and claims dependent thereupon, recitation of "hu3S193" is vague in the absence of recitation of deposit accession number or some other characteristic to clearly identify the intended antibody/hybridoma because, absent the recitation of identifying characteristics or a deposit accession number, it is not clear what structure and properties are encompassed by the named antibody.

In claims 5-8, improper Markush language is used to claim the members of the group. The alternatives "selected from...or" or "selected from the group consisting of...and" are acceptable.

Claims 13 and 14 are vague in the absence of recitation of deposit accession number to clearly identify the antibody/hybridoma because, absent the recitation of deposit accession numbers, it is not clear what structure and properties are encompassed by the named antibodies.

In claim 15 and claims dependent thereupon, the acronyms "Mab" or "Elisa" should be defined on first presentation. The interrelationships of the steps and components of the method are not clear because it is not clear: what is encompassed by an "Elisa" plate; if the anti-idiotype antibody is specific for an anti-Lewis Y specific monoclonal antibody or some other antibody;

what function is being performed by the secondary antibody because its specificity is undefined; or which of the previously recited antibodies is "the" antibody for which binding specificity is being evidenced. Moreover, recitation of "the" amount lacks antecedent basis.

In claim 16 it is not clear if hu3S193 is the control antibody because this is the only previously recited "Mab."

In claim 17 it is not clear how the anti-idiotype antibody is directed against Lewis Y antigen.

In claim 18 and claims dependent thereupon, the acronym "Elisa" should be defined on first presentation and is not clear as to what applicant intends as encompassed. The acronym "BSA" should be defined on first presentation. The interrelationships of the steps and components of the method are not clear because it is not clear: if the added anti-idiotype antibody is that of the preamble and specific for an anti-Lewis Y specific monoclonal antibody or some other antibody; how one detects binding in the absence if the anti-idiotype antibody is added in step b. Moreover, recitation of "the" binding, amount, presence, absence, and ability lack antecedent basis.

In claim 19, recitation of "anti- anti-" is vague and it is believed that only one "anti-" may have been intended.

In claim 21 and claims dependent thereupon, the acronym "Elisa" should be defined on first presentation and is not clear as to what applicant intends as encompassed. The acronym "BSA" should be defined on first presentation. The interrelationships of the steps and components of the method are not clear because it is not clear if the added anti-idiotype antibody is specific for a particular anti-Lewis Y specific monoclonal antibody suspected in the sample.

Moreover, recitation of "the" presence and amount lack antecedent basis and are not clear as to what is being detected, presence or amount.

In claim 23, the acronym "Elisa" should be defined on first presentation and is not clear as to what applicant intends as encompassed. The acronym "HAHA" should be defined on first presentation. The interrelationships of the steps and components of the method are not clear because it is not clear what is intended by "determining there from" or how this even relates to step b because no nexus is provided. Moreover, recitation of "the" presence or absence lack antecedent basis.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

(f) he did not himself invent the subject matter sought to be patented.

Claims 1-23 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Liu et al. (Hybridoma and Hybridomics 22: 219, July 2003).

Claims 1-23 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

Liu et al., having authorship different from the instant inventive entity, disclose the invention essentially as claimed.

Claims 1-3, 5-7, 9-11, 15 and 17 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Hirashima et al. (J. Immunol. 145: 224, 1990).

Hirashima et al. disclose monoclonal anti-idiotypic antibodies specific for an anti-Lewis Y monoclonal antibody. The specificity of the anti-idiotypic antibodies is tested by enzyme-linked immunosorbent assay with immobilized monoclonal anti-Lewis Y (see e.g. page 225, col. 1). The selected anti-idiotypic antibodies block the binding of the anti-Lewis Y antibody to Lewis Y antigen (see e.g. page 226, col. 1). Immunoassays using immobilized anti-idiotypic antibodies are taught.

Claims 1-3, 5-7, 9-11, 15, and 17 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Rosok et al. (J. Immunol. 160: 2353, 1998).

Rosok et al. disclose a monoclonal anti-idiotypic antibody specific for an anti-Lewis Y monoclonal antibody. The anti-idiotypic antibody is tested by enzyme-linked immunosorbent assay with immobilized or solution phase monoclonal anti-Lewis Y to test specificity and its ability to block the binding of the anti-Lewis Y antibody to Lewis Y antigen (see e.g. page 2354, col. 1, col. 2, and page 2355, col. 1). Immunoassays using antigen complexed to human serum albumin immobilized in microtiter plate wells are taught.

Claims 1-3, 5-7, 9-11, 15 and 17 are rejected under 35 U.S.C. § 102(e)(1) as being clearly anticipated by Eckert et al. (US 2002/0146410).

Eckert et al. disclose monoclonal anti-idiotypic antibodies specific for the BR55-2 anti-Lewis Y monoclonal antibody. The selected anti-idiotypic antibodies block the binding of the BR55 antibody to Lewis Y antigen (see e.g. [0035]). The specificity of the anti-idiotypic antibodies is tested by enzyme-linked immunosorbent assay with immobilized monoclonal BR55-5 F(ab')2 fragments (see e.g. page 8, Example 3). Immunoassays using immobilized anti-idiotypic antibodies are taught.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Armour et al. (US 5,874,060), Wallace et al. (US 6,310,185), LoBuglio (WO 90/06515), Rosok et al. (J. Immunol. 160: 2353, 1998), and Scott (Can. Res. 60: 3254, 2000).

Wallace et al. or Armour et al. teach humanized versions of the murine 3S193 anti-Lewis Y monoclonal antibody for detecting and/or treating cancer. The references do not teach anti-idiotype antibodies specific for the anti-Lewis Y antibody.

LoBuglio teaches methods for producing and screening monoclonal anti-idiotypic antibodies specific for an antibody of interest and teaches the use of such anti-idiotypic antibodies in sandwich assays for detection of an antibody reagent of interest (see e.g. pages 6-8) for purposes such as analysis of the pharmacokinetics of the antibody reagent (see e.g. page 1).

The teachings of Rosok et al. are as set forth previously in this Office action. Additionally, the reference teaches assays of antibody binding and antibody inhibition between the monoclonal antibody of interest and anti-idiotypic antibodies specific therefor on plates coated with the antigenic Lewis Y hapten coupled to protein. The reference teaches the frequent use of anti-idiotypic antibodies in support of clinical studies with therapeutic antibodies as well as alternatively as a vaccine treatment (see e.g. page 2353).

Scott et al. also teach the production of humanized murine 3S193 anti-Lewis Y monoclonal antibody for detecting and/or treating cancer. The reference teaches the availability of the Lewis Y antigen coupled to a bovine serum albumin carrier (see e.g. page 3255) for assays of, for example, antibody specificity.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have elicited anti-idiotypic antibodies specific for the humanized antibody taught in Armour et al., Wallace et al., and/or Scott et al. because this is conventional in the art for determinations of therapeutic antibodies in support of clinical studies as taught in LoBuglio and Rosok et al. One of ordinary skill in the art would have been motivated to use conventional

assays such as those taught in LoBuglio and Rosok et al. to obtain and characterize anti-idiotypic antibodies for use and would have been motivated to substitute available similar reagents, such as the available bovine serum albumin conjugates taught by Scott et al. for human serum albumin conjugates taught by Rosok et al., with an extremely reasonable expectation that the similar reagents would successfully perform their expected functions, such as providing immobilized antigens. It would have been further obvious to one of ordinary skill to have selected from notoriously old and well known labels, such as peroxidase labels, for immunoassays motivated by choice or available detection equipment.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Hellstrom et al. (US 5,89,045) teach monoclonal anti-idiotypic antibodies specific for an anti-Lewis Y monoclonal antibody (see cols. 67 and 76).

Hellstrom et al. (US 5,242,824) teach monoclonal anti-idiotypic antibodies specific for an anti-Lewis Y monoclonal antibody (see col. 8).

Huse et al. (US 2002/0146740) teach monoclonal anti-idiotypic antibodies specific for an anti-Lewis Y monoclonal antibody (see e.g. [0118]).

Ritter et al. (Can. Res. 61: 6851, 2001) teach BIACORE determinations of anti-humanized antibody responses.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, SPE, can be contacted at (571) 272-0806.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner, Art Unit 1641
March 31, 2010

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